REMARKS

Claims 64-105 are pending in the present application and at issue.

It is respectfully submitted that the present reply presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the following remarks is requested.

I. The Rejection of Claims 64-105 under 35 U.S.C. 112

The Office maintained the rejection of claims 64-95 under 35 U.S.C. 112, first paragraph, written description. This rejection is respectfully traversed.

Section 112, first paragraph provides that:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same....

The written description requirement of 35 U.S.C. § 112, first paragraph, is fulfilled when the patent specification describes the claimed invention in sufficient detail such that the claim limitations are described so that one of skill in the art would recognize that the applicants had invented the subject matter. See *Vas-Cath, Inc. v. Mahurkar*, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); *In re Herschler*, 200 U.S.P.Q. 711 (C.C.P.A. 1979). The written description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See *In re Marzocchi*, 169 U.S.P.Q. 367 (CCPA 1971).

The written description requirement can be met by showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics. See, e.g., *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398, 1404 (Fed. Cir. 1997); *Enzo Biochem v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002). A description of a claimed genus may be achieved by recitation of a representative number of species falling within the scope of the genus or by a recitation of structural features common to the members of the genus which constitute a substantial portion of the genus. See *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d at 1569.

The Patent Office's "Guidelines for the Examination of Patent Applications Under The 35 U.S.C. § 112, ¶ 1 'Written Description' Requirement" also provide guidance as to how to determine if there is sufficient written description to inform the artisan that the applicant was in possession of the claimed genus at the time the application was filed. These guidelines reiterate the Federal Circuit's law that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by relevant identifying characteristics, i.e., structure or other physical and/or chemical characteristics, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In particular, the PTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001). The Written Description Guidelines also state that a representative number of species requires that the species which are expressly described be representative of the entire genus. The Written Description Guidelines further state that what constitutes a representative number is an inverse function of the predictability of the art.

The claimed invention is drawn to variants of a laccase of SEQ ID NO: 10, comprising a substitution of the amino acid at position 119 with H, wherein the variant has laccase activity. Thus, the claims require that (1) the parent laccase is the laccase of SEQ ID NO: 10, (2) the variant comprises one or more specific substitutions at one or more specific positions, and (3) the variant has laccase activity. Because of these claim requirements, the claims provide both structural and functional limitations on the variants of the present invention.

Moreover, the specification specifically describes a number of other positions and mutations, which can be combined with the claimed substitutions. For example, at page 10, lines 28-35 and page 11, lines 30-37, the specification provides that the variants may further comprise a substitution at positions 364, 365, 366, 366, 368, 369, 370, 371, 372, 373, 426, 427, 429, 430, 431, 432, 503, 504, 505, 507, 508, 509, 511. 512, and 513.

Thus, the specification discloses numerous variants of the present invention and evidences that Applicants possessed these species. These species are a representative

number of species within the scope of the genus and therefore Applicants' disclosure evidences that Applicants were in possession of the claimed genus of variants at the time the application was filed.

Moreover, the level of skill in the art of enzyme variants is very high. Indeed, there are numerous U.S. patents on laccase variants comprising a mutation at one or more positions. Examples of recently-issued U.S. patents are U.S. Patent Nos. 5,770,419, 5,925,554, and 5,972,670, 5,998,353, and 6,277,611. It would be routine for one of ordinary skill in the art to combine the substitutions recited in the claims of the present application with any of the mutations described in the prior art. Applicants note that the claims of all of these patents use the transition term "comprising".

In sum, Applicants' specification provides (1) a precise definition by structure of the genus of laccase variants sufficient to distinguish it from other laccase variants and (2) a description of numerous representative members of the genus, in sufficient detail so that one of skill in the art would recognize that Applicants had invented the claimed subject matter. Accordingly, Applicants respectfully submit that the rejection as failing to comply with the written description requirement is improper.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claims 64 and 68 under 35 U.S.C. 102

Claims 64 and 68 are rejected under 35 U.S.C. 102(b) as being anticipated by Germann et al. (Proc. Natal. Acad. Sci., 83: 8854-8858 (1998)). This rejection is respectfully traversed.

Claims 64 and 58 read as follows:

> 64. A variant of a laccase, wherein the variant has laccase activity and comprises one or more of the following mutations:
> (a) H93E;
> (b) H95E;
> (c) D106A, D106F, D106I, D106L, D106P, D106V, D106W, or D106Y;
> (d) A108F, A108I, A108L, A108P, A108V, A108W, or A108Y;
> (e) N109A, N109D, N109F, N109I, N109L, N109P, N109Q, N109V, N109W, or N109Y;
> (f) T428A, T428F, T428I, T428L, T428P, T428V, T428W, or T428Y;
> (g) M433E;
> (h) L500F, L500I, L500W, or L500Y;
> (i) A506E;
> (j) S510A, S510F, S510I, S510L, S510P, S510V, S510W, or S510Y;

G511F, G511I, G511L, G511P, G511V, G511W, or G511Y; and
(l) G514A, G514F, G514I, G514L, G514P, G514V, G514W, or G514Y,
wherein the laccase has an amino acid sequence of SEQ ID NO: 10.

68. The variant of claim 64, which comprises A108F, A108I, A108L, A108P, A108V, A108W, or A108Y.

Thus, both claims require that the laccase of SEQ ID NO: 10 be modified by substitution of the amino acid residue at the specified positions with a specified amino acid residue.

Germann et al. disclose a wild-type laccase derived from *Neuropora crassa*. The *Neuropora crassa* laccase has not been modified by substitution at any position. Therefore, the laccase is not a variant.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 64-105 under 35 U.S.C. 112

Claims 64-105 are rejected under 35 U.S.C. 112, first paragraph, new matter, as failing to comply with the written description requirement. Specifically, the Office stated that "Claims 64 and 69 specify mutant N109D, which lacks support in the specification as originally filed...." This rejection is respectfully traversed.

Variants of the laccase of SEQ ID NO: 10, comprising the substitution N109D is supported at page 12, line 24 of the specification. Applicants therefore submit that this rejection has been overcome.

IV. The Rejection of Claims 64-105 under 35 U.S.C. 112

Claims 64-105 are rejected under 35 U.S.C. 112 first paragraph, enablement, "because the specification ... does not reasonably provide enablement for variant laccases having undefined or broadly defined structures." This rejection is respectfully traversed.

Section 112 of U.S. Patent Code requires that the specification be "enabling" to a person skilled in the art to which the invention pertains. "A specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which corresponds in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of section 112 unless there is reason to doubt the objective truth of the statements

contained therein which must be relied on for enabling support." *In re Marzocchi*, 169 U.S.P.Q. at 369.

It is also well settled that an assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974). See also *U.S. v. Telectronics*, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974); *Ex parte Hitzeman*, 9 U.S.P.Q.2d 1821 (BPAI 1988). In the absence of any evidence or apparent reason why compounds do not possess the disclosed utility, the allegation of utility in the specification must be accepted as correct. *In re Kamal*, 158 U.S.P.Q. 320 (C.C.P.A. 1968). See also *In re Stark*, 172 U.S.P.Q. 402, 406 n. 4 (C.C.P.A. 1972) (the burden is upon the Patent Office to set forth reasonable grounds in support of its contention that a claim reads on inoperable subject matter).

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). As stated in Wands, [w]hether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." See id. at 1404. The Wands factors which may be relevant for determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. Id.

In *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1976), the claimed process of preparing hydroperoxides used a metal salt complex as a catalyst. The specification disclosed catalysts that worked and some that gave little or no yield of hydroperoxides. The claims were rejected for lack of enablement, specifically as requiring undue experimentation to find useful catalysts. This rejection was reversed by the CCPA.

In holding that the claims did satisfy 35 U.S.C. 112, the Court observed, 190 U.S.P.Q. at 218:

> We cannot agree with the board that appellants' disclosure is not sufficient to enable one of ordinary skill in the art to practice the invention without undue experimentation. We note that many chemical processes, and catalytic processes particularly, are unpredictable, [citation omitted] and that the scope of enablement varies inversely with the degree of unpredictability involved, [citation

> omitted]. That this particular process is unpredictable is demonstrated further by appellants in their specification. Appellants have disclosed forty examples; one of these examples yields no hydroperoxides in the final product. Also, appellants have expressly indicated in their specification that some of these organometallic complex catalysts 'yield *** no hydroperoxides in the final product.'
>
> Appellants have apparently not disclosed every catalyst which will work; they have apparently not disclosed every catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with 'thousands' of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid 'literal' infringement of such claims by merely finding another analogous catalyst complex which could be used in 'forming hydroperoxides.'

The Court, 190 U.S.P.Q. at 218, recognized that some experimentation might be necessary for the skilled worker to select non-exemplified catalysts for use:

> Appellants have, in effect, provided those skilled in this art with a large but finite list of transition metal salts from which to choose in preparing such a complex catalyst. Appellants have actually carried out 40 runs using various transition metal salts and hexaalkylphosphoramides. If one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs, he would merely read appellants' specification for directions how to make and use the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed. The process discovered by appellants is not complicated, and there is no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. One skilled in this art would merely have to substitute the correct mass of a transition metal salt for the transition metal salts disclosed in appellants' 40 runs. Thus, we have no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst complexes within the scope of the claims work to produce hydroperoxides and which do not.

However, while some experimentation might be necessary, as long as the experimentation was not "undue experimentation," the claims would not violate 35 U.S.C. 112, *Angstadt*, Id.

> Since appellants have supplied the list of catalysts and have taught how to make and how to use them, we believe that the experimentation required to determine which catalysts will produce hydroperoxides would not be undue and certainly would not 'require ingenuity beyond that to be expected of one of ordinary skill in the art.' (Emphasis added).

As discussed above, the claimed invention is drawn to laccase variants of SEQ ID NO: 10, comprising a substitution of the amino acid at specified positions with specified amino acids, wherein the variant has laccase activity. Thus, the claims require that (1) the parent laccase is the laccase of SEQ ID NO: 10, (2) the laccase variant comprises a specific substitution at a specific position, and (3) the laccase variant has laccase activity. Because of these claim requirements, the claims provide both structural and functional limitations on the laccase variants of the present invention.

Moreover, as stated above, the specification specifically describes a number of other positions and mutations, which can be combined with the claimed substitutions. For example, at page 10, lines 28-35 and page 11, lines 30-37, the specification provides that the variants may further comprise a substitution at positions 364, 365, 366, 366, 368, 369, 370, 371, 372, 373, 426, 427, 429, 430, 431, 432, 503, 504, 505, 507, 508, 509, 511, 512, and 513.

Thus, the specification discloses a large number of laccase variants of the present invention, and illustrates how the laccase variants are made and used. While some experimentation might be necessary to identify other non-exemplified laccase variants, such experimentation would require carrying out a simple process without special equipment or unusual reaction conditions. This experimentation, if required, would not be undue and certainly would not require ingenuity beyond that expected of one of ordinary skill in the art. Certainly, there is no evidence of record to the contrary.

Moreover, the level of skill in the art of enzyme variants is very high. Indeed, there are numerous U.S. patents on laccase variants comprising a mutation at one or more positions. Examples of recently-issued U.S. patents are U.S. Patent Nos. 5,770,419, 5,925,554, 5,972,670, 5,998,353, and 6,277,611. It would be routine for one of ordinary skill in the art to combine the substitutions recited in the claims of the present application with any of the mutations described in the prior art. Applicants note that the claims of all of these patents use the transition term "comprising".

In sum, the specification contains a teaching of the manner and process of making and using the invention in terms which corresponds in scope to the claimed subject matter. Accordingly, the specification contains an enabling disclosure of the claimed invention.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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